REMARKS

In the claims

Claims 18–39 are currently pending with claims 27–39 withdrawn due to restriction/ election and claims 1–17 canceled without prejudice or disclaimer. Claims 18–26 are currently being examined on their merits.

Claim Amendments

Amended claim 18 has been amended according to the Examiner's suggestion and is fully supported by the specification, as originally filed.

Sequence compliance

Sequence identifier numbers are not necessary for page 28 since a skilled worker can easily figure out the sequence from the totality of the disclosure.

Rejections under 35 U.S.C § 112, second paragraph

Claim 18 stands rejected under 35 U.S.C § 112, second paragraph as allegedly being indefinite with respect to recitation of the term "gene expression of a polypeptide." It is respectfully submitted the term is not indefinite insofar as one of ordinary skill in the art would explicitly understand that the scope of the compounds being encompassed by such claim language. However, in order to expedite prosecution, Applicants have amended the claim.

The Office Action further alleges that the method encompassed by claim 18 "lacks essential steps" because "applicants have not set up any control steps to account for endogenous glucose dehydrogenases present in transformants comprising the fusion protein."

Applicants courteously disagree with this assertion.

> It is the function of the descriptive portion of the specification and not that of the claims to set forth operable proportions and similar process parameters and that claims are not rendered indefinite by the absence of the recitation of such limitations.

See *Ex parte Jackson*, 217 USPQ 804 (BPAI 1982).

> It is implicit in the claims that the conditions of the process have not been met unless the catalyst is present and active as a catalyst. Requiring a recitation in the claims of the specific deuterium peroxide proportions employed in the examples to insure that activity would be an unnecessary limitation. Disclosure in the *specification* sufficient to enable practice of the invention by one skilled in the art, taking into consideration obvious modifications of the reactant ratios of specific examples, is all that is required.

See *Dinh-Nguyen*, supra.

Accordingly, requiring such reaction conditions such as control steps, etc. in the claims is contrary to the cases cited above and even well established PTO practice.

Applicants respectfully submit that the claimed process may be accomplished by the use of a variety of reagents and/or steps that one of ordinary skill in the art can determine without undue experimentation. Additionally, Applicants provide extensive guidance on pages 17–21 and provide Examples 4–8, which would sufficiently enable one of ordinary skill in art to practice the claimed invention without additional burden resulting from undue experimentation. Limiting the claims to specific steps is not necessary as the invention is not so limited. Applicants' process claims provide enough clarity so that one of ordinary skill in the art needs no more than familiarity with routine laboratory protocol to determine whether a given experiment is within or outside the scope of the process claims. Further, prior art, such as the Yamada and Yamanishi references cited herein, verify that information relating to techniques for assaying presense of enzymes was readily available to one of ordinary skill in the art. Therefore, the claims are not indefinite as alleged by the Office Action.

Moreover, the rejected claim terms are common terms used in numerous patents issued by the PTO, i.e., the language used by applicants is common and accepted claim language under USPTO practice. A quick search can easily verify this.

Rejection under 35 U.S.C § 112, first paragraph

The rejection of claims 18–26 under 35 U.S.C § 112, first paragraph as allegedly lacking a written description is respectfully traversed.

In the rejection, the Examiner argues that there is no support for the recitation of the range for "variants, recombinants, and mutants" of glucose dehydrogenase. However, to satisfy the written description requirement, all that is needed is for the disclosure to "reasonably convey" that applicants' had possession of the claimed subject matter at the time of filing. See, e.g., *In re Kaslow,* 217 USPQ 1089 (Fed. Cir. 1982).

Regarding the objection pertaining to the alleged "lack of support for the use of a genus of polypeptides based on the disclosure pertaining to a single species (SEQ ID NO.:1)", Applicants respectfully submit that the specification both generically and specifically outlines the structural and functional aspects of the claimed glucose dehydrogenase fusion proteins. For example, at page 1, it is taught that "GlcDH or the sequence having the biological activity of GlcDH assumes the role of a marker or detector protein." The specification at page 6, lines 11–25 outlines the biochemistry of native GlcDH, and the utility of GlcDH in fusion proteins is provided at page 10, lines 11–33 of the instant specification. The assay techniques and the operative methods, including methods for isolation and purification of the claimed fusion proteins are provided in the various Examples contained in the specification. See Examples 1–8 of the instant application. Using this disclosure and the general knowledge of protein chemistry, one of ordinary skill could routinely screen for variants of the GlcDH, either in native or fused form, which constitute the desired activity. For example, if the operative methods are geared towards biochemical analysis, then one of ordinary skill could routinely utilize a GlcDH variant with the desired biochemical characteristics (stability, solubility, activity etc.). If the methods are geared towards cell-based assays then using routine techniques, one of ordinary skill in the art could utilize variants that offer desired expression and/or activity in cell-based assays. It is respectfully submitted that the specification reasonably conveys to one of ordinary skill in the art that the use of such variants or fragments is permissible inasmuch such fragments/variants have the desired GlcDH activity, which can be measured via routine procedures. The specific recitation of the structural elements, including amino acid sequences, is not required *per se* to practice the instant invention.

Applicants also disagree with the Examiner's assertion at page 6 of the open Office Action, that the specification fails to "recite additional species as encompassed by the claims." It is respectfully submitted that the mere recitation of "glucose dehydrogenase" is sufficient for understanding what structural and/or functional aspects are encompassed. *Ipsis verbis* recitation of other members of the claimed genus, such as variants and homologs, would constitute nothing more than what is already encompassed by the instant invention.

In view of the above remarks, it is respectfully submitted that applicants' disclosure more than reasonably conveys to one of ordinary skill in the art that, as of the filing date, Applicants' had possession of the claimed subject matter. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C § 103(a)

Claims 18–26 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Section II of *Current Protocols in Molecular Biology* (Kain & Ganguly, **1996**) in view of Yamada et al. (*Journal of Biological Chemistry*, **vol. 268**, pages: 12812–17, **1993**) and Yamanishi et al. (US 4,622,296). Withdrawal of the rejection is respectfully requested.

Kain and Ganguly generically describe a reporter system comprising a reporter gene (such as CAT, β-galactosidase, and luciferase) fused with a promoter sequence of interest, and assaying for the activity of a promoter using enzymatic or immunological detection methods (see, the 3rd paragraph of section 9.6.1, supplement 68 of the cited reference). Table 9.6.1 provides examples of such reporter genes. Supplement 29 in Section 9.6.4 of the cited reference outlines a method for designing such reporter vectors and outlines *in vitro* assays for quantifying reporter proteins. The cited reference makes no reference of fusion proteins, let alone disclose a method of assaying for the presence of a polypeptide of interest using a fusion protein comprising glucose dehydrogenase and said polypeptide of interest. In other words, the system and methods disclosed by Kain and Ganguly do not encompass or suggest all the aspects of the instant invention.

Yamada et al. describe topological structures of quinoprotein glucose dehydrogenase in *Escherichia coli* and its ubiquinone-binding site. See the Title and Abstract sections of Yamada et al. In the Materials and Methods section at page 12813, Yamada describe a fusion protein comprising glucose dehydrogenase and a screening protein such as alkaline phosphatase (AP) or β-galactosidase (GAL). The cited teaching utilizes the AP or GAL-based assays and substrates to screen for colonies expressing *E. coli* glucose dehydrogenase. See the section on *Enzymatic Assays* at page 12814 of the cited reference. In summary, Yamada does not describe a system or a method that encompasses the functional limitations of the instant invention.

The cited teachings of Yamanishi describe a process for measuring the activity of a dehydrogenase (more specifically, lactate dehydrogenase) employing a reaction stopper. See the Title and Abstract sections of Yamanishi et al. It is disclosed that such dehydrogenases could comprise one or more of the following enzymes: lactate dehydrogenase (LDH), glucose-6-phosphate dehydrogenase, glycerol-3-phosphate dehydrogenase, α-hydroxybutyrate dehydrogenase, 3α-hydroxysteroid dehydrogenase. The method utilizes a coupling reaction, whereby said dehydrogenase is coupled with a hydrogen acceptor (either NAD or NADP) and the activity of said dehydrogenase is measured using a UV/colorimetric assay. See, col. 1, paragraphs 2–3 of Yamanishi et al. Yamanishi does not disclose fusion proteins in general, or assay methods devoted to the measurement of the activity of fusion proteins comprising dehydrogenases. More specifically, the cited reference makes no mention of glucose dehydrogenase fusion proteins of the instant invention. As such, Yamanishi's teachings do not encompass either the structural or the functional limitations of the instant invention.

To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438

(Fed. Cir. 1991). See MPEP Section 2143 - Section 2143.03 for decisions pertinent to each of these criteria.

As previously outlined, the cited teachings of Kain & Ganguly, Yamada and Yamanishi do not encompass all the structural and/or functional limitations of the method claimed by the instant invention. As such, one of ordinary skill in the art would not be able to reformulate the instant invention by merely combining the cited references. Furthermore, neither the Office Action nor the cited teachings themselves offer any rationale as to why one of ordinary skill in the art would be motivated to combine the cited teachings. Kain's disclosure is drawn to reporter systems (i.e. genes), Yamada's teachings are drawn to AP or GAL-based detection methods, while Yamanishi's disclosure is drawn to native dehydrogenases. The cited teachings fail, either solely or in combination, to encompass what is claimed by the instant invention. The Office Action has not met the abovementioned criteria for *prima facie* case of obviousness. As such, withdrawal of the rejection is respectfully requested.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response to Deposit Account No. 13-3402.

Respectfully submitted,

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